

REMARKS

Claims 1, 4-6, 8-28, and 30-36 were pending at the time of the Office Action. Claims 33 and 34 stand withdrawn from consideration. Claims 1, 4-5, 8-15, and 35 stand rejected under 35 U.S.C. § 102, and all claims stand rejected under 35 U.S.C. § 103. Claims 1, 6, 8-28, 30-32, and 36 are also provisionally rejected for nonstatutory obviousness-type double patenting. Applicant addresses these rejections as follows.

Examiner Interview

Applicant thanks Examiner Mi and Supervisory Examiner McKelvey for the productive in-person interview conducted on November 2, 2010. Below, Applicant provides a summary of the claim amendments and issues discussed during the interview.

Claim Amendments

Claim 1 has been amended to feature a method for treating a keratosis lesion of the skin of a patient by topically administering to the lesion a pharmaceutically effective amount of a polyphenol composition comprising (i) a mixture of polyphenols and (ii) a carrier, wherein the composition includes from about 5% (w/w) to about 20% (w/w) of the polyphenol mixture, which itself includes the components, epicatechol, epicatechol gallate, epigallocatechol, epigallocatechol gallate, and gallocatechol. Support for this amendment is found, for example, in original claim 35, and at page 5, lines 29-30, page 10, lines 11-13, page 14, lines 17-20, and page 17, lines 1-2, of the parent PCT specification (PCT/EP2004/0113000). Further, claims 4 and 5 have been cancelled, and claim 35 has been amended to specify particular forms of keratoses. In addition, new claims 37-39 have been added. Support for these claims is found throughout the parent PCT specification (PCT/EP2004/0113000), for example, as follows: claim 37, page 14, lines 15-20; claim 38, page 19, lines 18-20; and claim 39, Examples 1 and 2.

The present amendments were made without prejudice and solely to expedite prosecution, and Applicant reserves the right to pursue any cancelled subject matter in this or in a continuing application. No new matter has been added by these amendments.

Rejection under 35 U.S.C. § 102

Claims 1, 4-5, 8-15, and 35 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Lou et al., (*Proc. of the American Assoc. for Cancer Res.* 43: 1143, 2002). As applied to the present claims, this rejection is respectfully traversed.

Amended claim 1 features a method for treating a keratosis lesion of the skin of a patient by topically administering to the lesion a pharmaceutically effective amount of a polyphenol composition comprising (i) a mixture of polyphenols and (ii) a carrier, wherein the composition includes from about 5% (w/w) to about 20% (w/w) of the polyphenol mixture, which itself includes the components, epicatechol, epicatechol gallate, epigallocatechol, epigallocatechol gallate, and gallocatechol. As discussed and agreed at the recent Examiner Interview, Lou does not disclose treatment of a keratosis lesion. The rejection of present claims 1, 4-5, 8-15, and 35 under 35 U.S.C. § 102(b) may be withdrawn.

Rejections under 35 U.S.C. § 103

Claims 1, 4-6, 8-32, and 30-36 also stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Lou in view of either Brash et al. (U.S. Patent Application Publication No. 2002/0198161; herein “Brash”) and Voet (U.S. Patent No. 6,723,750; herein “Voet”); An (*Photochem and Photobiol.* 76: 73-80, 2002); or Katiyar (*Curr. Drug Targets-Immune, Endocrine, & Metabol. Disorders*, pp. 234-242, 2003). These rejections are respectfully traversed.

As discussed above, Applicant has amended independent claim 1 to feature a method for treating a keratosis lesion of the skin of a patient by topically administering to the keratosis lesion a pharmaceutically effective amount of a polyphenol composition

comprising (i) a mixture of polyphenols and (ii) a carrier, wherein the composition includes from about 5% (w/w) to about 20% (w/w) of the polyphenol mixture, which itself contains the components, epicatechol, epicatechol gallate, epigallocatechol, epigallocatechol gallate, and gallocatechol. Such a treatment is nowhere taught by Lou. As acknowledged by the Office, Lou instead discusses only squamous cell papillomas, keratoacanthomas, and squamous cell carcinomas, skin disorders very different from keratoses in their pathology. One skilled in the art reading Lou's results would not reasonably conclude that topical application of a mixture of polyphenols to keratoses would result in improvement of that distinct condition. Nor would the results disclosed in Lou provide the requisite reasonable expectation of success for the present claims directed to treating keratoses. Lou on its own therefore does not form the basis of a *prima facie* case of obviousness for independent claim 1 or its dependent claims.

Moreover, this deficiency in Lou is not cured by any of the secondary references cited by the Office. Taken in turn, neither Brash nor Voet discusses polyphenolic compounds for treating keratoses. Brash teaches that skin precancers may be treated topically with an unrelated sulfuric compound, while Voet teaches curettage for treating cancerous or pre-cancerous skin lesions. Accordingly, the § 103 rejection as applied to claims 1, 4-6, 8-15, 27, 28, 30-32, and 35 in view of the combination of Lou, Brash, and Voet may be withdrawn.

In like manner, the secondary reference An does not teach or suggest the treatment of keratoses in a patient. An describes basic experiments that measure COX-2 expression in cells excised from various skin lesions, including actinic keratoses. These keratoses were not treated in any way. In addition, in separate experiments, An looks at the potential for preventive effects of green tea extracts. An teaches the topical administration of a green tea polyphenol (GTP) extract to murine or human skin prior to UVB irradiation. An fails to teach or suggest that the GTP extract treats an established keratosis. Indeed, An states (pages 78-79):

[T]he observed decrease in COX-2 expression in both murine and human skin receiving a topical application of GTP suggests that GTP may act as a

chemopreventive agent by blocking this target.

Accordingly, An fails to teach or suggest that polyphenolic compounds would treat keratosis lesions. Neither does An provide a reasonable expectation of success for this outcome. Applicant respectfully requests that the § 103 rejection of claims 1, 4-6, 8-15, 35, and 36 also be withdrawn.

The final reference cited by the Office is Katiyar. This paper, while providing an overview of work in the field of prevention of skin damage with various green tea components, fails to discuss treatment of keratoses. As above, Applicant submits that a combination of Lou and Katiyar does not support a *prima facie* case of obviousness and requests reconsideration and withdrawal of the § 103 rejection of claims 1, 4-6, 8-26, and 35.

Provisional Double-Patenting Rejection

Claims 1, 6, 8-32, and 36 stand provisionally rejected for obviousness-type double patenting over claims 1-6, 8, 16, 18, 23-27, and 30-33 of co-pending U.S. Patent Application Serial No. 10/682,612. Applicant requests that this rejection be held in abeyance until the currently pending claims and those of the '612 application have been found allowable except for this ground of rejection.

CONCLUSION

Applicant submits that the claims are now in condition for allowance, and such action is respectfully requested. Transmitted herewith is a Petition to extend the period for replying to the Office Action for three months, to and including November 17, 2010, and payment of the required extension fee.

If there are any other charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

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